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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.	
10/036,729	12/21/2001	Jaap M. Middeldorp	9310-13DVCTDV	6359	
	7590 10/16/2007 L SIBLEY & SAJOVEC	EXAMINER			
PO BOX 37428 RALEIGH, NC 27627			LI, QIAN JANICE		
			ART UNIT	PAPER NUMBER	
			1633	<u> </u>	
			MAIL DATE	DELIVERY MODE	
·			10/16/2007	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

		i	
	Application No.	Applicant(s)	
*	10/036,729	MIDDELDORP ET AL.	
Office Action Summary	Examiner	Art Unit	
	Q. Janice Li, M.D.	1633	
The MAILING DATE of this communication app Period for Reply	pears on the cover sheet with the	correspondence address	
	VIC CET TO EVOIDE 2 MONTU	VS) OR THIRTY (20) DAVE	
A SHORTENED STATUTORY PERIOD FOR REPL' WHICHEVER IS LONGER, FROM THE MAILING DA - Extensions of time may be available under the provisions of 37 CFR 1.1 after SIX (6) MONTHS from the mailing date of this communication. - If NO period for reply is specified above, the maximum statutory period of - Failure to reply within the set or extended period for reply will, by statute - Any reply received by the Office later than three months after the mailing earned patent term adjustment. See 37 CFR 1.704(b).	ATE OF THIS COMMUNICATIO 36(a). In no event, however, may a reply be ti will apply and will expire SIX (6) MONTHS from a cause the application to become ABANDONI	N. Imely filed In the mailing date of this communication. ED (35 U.S.C. § 133).	
Status			
1)⊠ Responsive to communication(s) filed on 23 Ju	ulv 2007.		
•	action is non-final.		
3) Since this application is in condition for allowa	nce except for formal matters, pr	osecution as to the merits is	
closed in accordance with the practice under E	Ex parte Quayle, 1935 C.D. 11, 4	53 O.G. 213.	
Disposition of Claims	•	æ .	
4)⊠ Claim(s) <u>6-9,26,27 and 32-34</u> is/are pending ir	the application.		
4a) Of the above claim(s) is/are withdraw			
5) Claim(s) is/are allowed.			
6)⊠ Claim(s) <u>6-9,26,27 and 32-34</u> is/are rejected.			
7) Claim(s) is/are objected to.			
8) Claim(s) are subject to restriction and/o	r election requirement.		
Application Papers			
9) The specification is objected to by the Examine	ar ·		
10) The drawing(s) filed on is/are: a) acc		Examiner.	
Applicant may not request that any objection to the			
Replacement drawing sheet(s) including the correct		·	
11) The oath or declaration is objected to by the Ex			
Priority under 35 U.S.C. § 119			
12) Acknowledgment is made of a claim for foreign	priority under 35 U.S.C. & 1196	a)-(d) or (f)	
a) ☐ All b) ☐ Some * c) ☐ None of:	i priority under oo o.o.o. 3 i rott	2) (2) 3. (.).	
1. Certified copies of the priority document	s have been received.		
2. Certified copies of the priority document		tion No	
3: Copies of the certified copies of the prio	• •		
application from the International Burea	u (PCT Rule 17.2(a)).		
* See the attached detailed Office action for a list	of the certified copies not receive	red.	
		•	
Attachment(s)			
1) Notice of References Cited (PTO-892)	4) Interview Summar		
2) Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail [Date	
3) Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date	5)	ratent Application	
,	 - 		

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DETAILED ACTION

The amendment and response filed 7/23/2007 are acknowledged. Claim 34 has been amended. Claims 6-9, 26, 27, 32-34 are pending and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims or persuasive arguments will not be reiterated. The arguments in 7/23/07 response would be addressed to the extent that they apply to current rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6, 9 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the remarks, the applicant first asserts,

In claim 6, the nucleic acid sequences encode peptides comprising an epitope of the VCA-p18 or VCA-p40 protein.

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on/Control Number: 10/030,72

In response, it is noted claim 6 as written, the nucleic acid sequence encodes a peptide that is immunochemically reactive with antibodies to VCA-18 or VCA-p40. Hence, the genus embraced by the claimed nucleic acids may encompass coding sequences for peptides comprising an epitope of the VCA-p18 or VCA-p40, but they are not limited by such coding sequence, rather the genus encompasses nucleic acid sequences encoding any protein as long as it is immunochemically reactive with antibodies to VCA-18 or VCA-p40, which include proteins having no clear relationship to VCA proteins. Claim 6 contains multiple phrases further limiting the antibodies, but not further limiting the peptide itself. The only limitation to the peptide is its immunochemical reactivity to the antibodies. One cannot extrapolate the structures of the protein genus from the immune reactivity.

Applicants then argues that the antibodies are further defined by particular hybridoma, and one of skill in the art further recognizes that monoclonal antibodies are specific to a single epitope and all of the antibodies produced from a single hybridoma are identical.

In response, it is noted that the antibodies are not limited by the recited hybridomas, but rather limited by the immunochemical reactivity: "are antibodies having the same reactivity with VCA-p18 as antibodies produced by the hybridoma...".

Even assuming *arguendo* claims are directed to peptides reactive with the antibodies produced by the recited hybridoma, the peptides encompass a genus of amino acid sequences, whose nucleic acid coding sequences are limited only by the fact that they <u>contain</u> a nucleotide, whose expression product has certain immune

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reactivity, while since there is no length limitation on the nucleic acid sequences, they could be a genomic sequence or a fusion protein sequence, or any other known or unknown nucleic acid sequences that happen to encode a protein reactive to the antibodies or contain sequences sharing homology with SEQ ID Nos: 1 and/or 3. Thus, even if the antibodies produced by the hybridoma have the same reactivity with VCA-18 or VCA-40, the proteins reactive to the antibodies may be structurally distinct. This could be seen in the example of the specification, where serum proteins reactive with applicant's antibody have different domain combinations, i.e structurally different (see e.g. table I of the specification).

Applicants then argue that the specification demonstrates actual reduction to practice of the nucleic acids of claim 6 as exemplified by peptides represented by various SEQ ID Nos: 2, 4, 5, 6, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 and 22.

In response, it is noted that majority of the numbered peptides are only a partial sequence of a protein, which each has an amino acid sequence distinct from the other, yet they all demonstrated immune reactivity with a VCA-p18 antibody. Among the 15 proteins listed in table I, only proteins from serum No. 9 and 10 have the same combination of domains I, II, & III, yet still it's unclear whether they have the same protein sequences in the remaining portion of the immune reactive protein. One skilled in the art could not extrapolate the full-length protein sequences from the disclosure of the partial sequences and their immune reactivity. Thus, working examples of the specification, especially table I further supports the Office position, the specification fails

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to provide an adequate description for the genus of the nucleic acid sequences encompassed by the claims.

An adequate written description for a genus of nucleic acid sequences encompassed by instant claims requires more than a mere statement that they are part of the invention, what is required is a description of the sequences themselves. The court has made it very clear "Conception of Chemical Compound Requires That Inventor BE ABLE TO DEFINE COMPOUND SO AS TO DISTINGUISH IT FROM OTHER MATERIALS, AND TO DESCRIBE HOW TO OBTAIN IT, RATHER THAN SIMPLY DEFINING IT SOLELY BY ITS PRINCIPAL BIOLOGICAL ACTIVITY". Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016 (Fed. Cir. 1991).

The Revised Interim Guidelines state "The Claimed Invention as a whole may not be adequately described if the Claims require an essential or critical element which is not adequately described in the specification and which is not conventional in the art" (Column 3, page 71434), "when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus", "In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus" (Column 2, page 71436).

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "APPLICANT MUST CONVEY WITH REASONABLE CLARITY TO THOSE SKILLED IN THE ART THAT, AS OF THE FILING DATE SOUGHT, HE OR SHE WAS IN POSSESSION OF THE INVENTION. THE INVENTION IS, FOR PURPOSES OF THE 'WRITTEN DESCRIPTION' INQUIRY, WHATEVER IS NOW CLAIMED." (See page 1117.) The

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specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the genus sequences encompassed by the claims. Therefore, for reasons of record and set forth *supra*, the rejection stands.

Claims 6, 9 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record and set forth *supra*.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 6-9, 26, 27, 32-34 <u>stand</u> rejected under 35 U.S.C. 102(b) as being anticipated by *Laux et al.* (The EMBO J 1988;7:769-74).

Laux et al. teaches a nucleic acid sequence comprising a subsequence of instant SEQ ID No: 1 (residues 1-535 of SEQ ID No: 1), which encodes at least 12 contiguous amino acids of EBV VCA-p18 (the amino acid sequence SEQ No: 5), which would be immunochemically reactive with antibodies to the EBV VCA-p18. Laux et al. also teaches a nucleic acid sequence comprising instant SEQ ID No: 3, which encodes 12 contiguous amino acids of an EBV VCA-40. Laux et al. discloses a vector comprising the sequences (e.g. fig. 1). Accordingly, Laux et al. anticipates instant claims.

In the remarks, the applicant asserts that multiple alignments were performed and homology as stated in the Office action was not found.

In response, the printed copy of the database search result is hereby enclosed, which contains the details of the alignment.

Claims 6-9, 26, 27, 32-34 stand rejected under 35 U.S.C. 102(b) as being anticipated by *Bankier et al.* (Mol Biol Med 1983;1:425-445).

Bankier et al. teaches a nucleic acid sequence comprising a subsequence of instant SEQ ID No: 1 (residues 1-535 of SEQ ID No: 1), which encodes at least 12 contiguous amino acids of EBV VCA-p18 (the amino acid sequence SEQ No: 5), which would be immunochemically reactive with antibodies to the EBV VCA-p18. Bankier et al. also teaches a nucleic acid sequence comprising a sequence that shares 98.8%

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homology with instant SEQ ID No: 3 (subsequence thereof), which encodes 12 contiguous amino acids of an EBV VCA-40. *Bankier et al.* discloses that the sequences were cloned in a vector (e.g. figs. 1-3). Accordingly, *Bankier et al.* anticipates instant claims.

In the remarks, the applicant asserts that multiple alignments were performed and homology as stated in the Office action was not found.

In response, the printed copy of the database search result is hereby enclosed, which contains details of the alignment.

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is **571-272-0730**. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The **fax** numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547. For all other customer support, please call the USPTO Call Center (UCC) at **800-786-9199**.

Q. JANICE LI, M.D. PRIMARY/EXAMINER

Q Járiice Li, M.D. Primary Examiner Art Unit 1633

QJL October 10, 2007

SCORE Search Results Details for Application 10036729 and Search Result \$\\$itemName. Page 6 of 16

661 CACTCGGGGCCTTACGGATTTCA¢CCTCATCAAAGCTA¢GAAGTGCCCAGATACGTCCCT 720 Qу Db 137078 CACTCGGGGCCTTACGGATTTCAGCCTCATCAAAGCTACGAAGTGCCCAGATACGTCCCT 137137 721 CATCCGCCCCACCACCAACTTCTCACCAGGCAGCTCAGGCGCAGCCTCCACCCCGGGC 780 Qу 137138 CATCCGCCCCACCACCACCTTCTCACCAGGCAGCTCAGGCGCAGCCTCCACCCCGGGC 137197 Db 781 ACACAGGCCCCGAAGCCCACTGTGTGGCCGAGTCCACGATCCCTGAGGCGGGAGCAGCC 840 Qу Db 137198 ACACAGGCCCCCGAAGCCCACTGTGTGGCCGAGTCCACGATCCCTGAGGCGGGAGCAGCC 137257 Qу 841 GGGAACTCTGGACCCCGGGAGGACACCAACCCTCAGCAGCCCACCACCGAGGGCCACCAC 900 137258 GGGAACTCTGGACCCCGGGAGGACACCCAACCCTCAGCAGCCCACCACCGAGGGCCACCAC 137317 Db 901 CGCGGAAAGAACTGGTGCAGGCCTCTGCGTCCGGAGTGGCTCAGTCTAAGGAGCCCACC 960 Qy 137318 CGCGGAAAGAAACTGGTGCAGGCCTCTGCGTCCGGAGTGGCTCAGTCTAAGGAGCCCACC 137377 Db 961 ACCCCCAAGGCCAAGTCTGTGTCAGCCCACCTCAAGTCCATCTTTTGCGAGGAATTGCTG 1020 Qу Db 137378 ACCCCCAAGGCCAAGTCTGTGTCAGCCCACCTCAAGTCCATCTTTTGCGAGGAATTGCTG 137437 Qy 1021 AATAAACGCGTGGCTTGA 1038 Db 137438 AATAAACGCGTGGCTTGA 137455 RESULT 7 EBV LOCUS 172281 bp DNA circular VRL 18-APR-2005 DEFINITION Epstein-Barr virus (EBV) genome, strain B95-8. ACCESSION V01555 J02070 K01729 K01730 V01554 X00498 X00499 X00784 VERSION V01555.1 GI:59074 **KEYWORDS** DNA polymerase; EBNA; genome; ribonucleotide reductase; tandem repeat; terminal repeat. SOURCE Human herpesvirus 4 (Epstein-Barr virus) ORGANISM Human herpesvirus 4 Viruses; dsDNA viruses, no RNA stage; Herpesviridae; Gammaherpesvirinae; Lymphocryptovirus. REFERENCE **AUTHORS** Arrand, J.R., Rymo, L., Walsh, J.E., Bjorck, E., Lindahl, T. and Griffin, B.E. TITLE Molecular cloning of the complete Epstein-Barr virus genome as a set of overlapping restriction endonuclease fragments JOURNAL Nucleic Acids Res. 9 (13), 2999-3014 (1981) PUBMED 6269068 REFERENCE 2 AUTHORS Kozak, M. TITLE Possible role of flanking nucleotides in recognition of the AUG initiator codon by eukaryotic ribosomes JOURNAL Nucleic Acids Res. 9 (20), 5233-5252 (1981) PUBMED 7301588 REFERENCE AUTHORS Deininger, P.L., Bankier, A., Farrell, P., Baer, R. and Barrell, B. TITLE Sequence analysis and in vitro transcription of portions of the Epstein-Barr virus genome JOURNAL J. Cell. Biochem. 19 (3), 267-274 (1982) PUBMED 6296170 REFERENCE

```
AUTHORS
             Farrell, P.J., Bankier, A., Seguin, C., Deininger, P. and Barrell, B.G.
   TITLE
             Latent and lytic cycle promoters of Epstein-Barr virus
   JOURNAL
             EMBO J. 2 (8), 1331-1338 (1983)
    PUBMED
             10872327
 REFERENCE
             Farrell, P.J., Deininger, P.L., Bankier, A. and Barrell, B.
   AUTHORS
             Homologous upstream sequences near Epstein-Barr virus promoters
   TITLE
   JOURNAL
             Proc. Natl. Acad. Sci. U.S.A. 80 (6), 1565-1569 (1983)
    PUBMED
             6300857
 REFERENCE
             6
                (bases 142687 to 159853)
             Bankier, A.T., Deininger, P.L., Farrell, P.J. and Barrell, B.G.
   AUTHORS
   TITLE
             Sequence analysis of the 17,166 base-pair EcoRI fragment C of B95-8
             Epstein-Barr virus
   JOURNAL
             Mol. Biol. Med. 1 (1), 21-45 (1983)
    PUBMED
             6092825
REFERENCE.
                (bases 112620 to 125316)
   AUTHORS
             Seguin, C., Farrell, P.J. and Barrell, B.G.
   TITLE
             DNA sequence and transcription of the BamHI fragment B region of
             B95-8 Epstein-Barr virus
   JOURNAL
             Mol. Biol. Med. 1 (3), 369-392 (1983)
    PUBMED
             6094953
REFERENCE
                (bases 45644 to 52450)
  AUTHORS
             Jeang, K.T. and Hayward, S.D.
   TITLE
             Organization of the Epstein-Barr virus DNA molecule. III. Location
             of the P3HR-1 deletion junction and characterization of the NotI
             repeat units that form part of the template for an abundant
             12-O-tetradecanoylphorbol-13-acetate-induced mRNA transcript
   JOURNAL
             J. Virol. 48 (1), 135-148 (1983)
    PUBMED
             6310141
REFERENCE
                (bases 159853 to 172281)
   AUTHORS
             Bankier, A.T., Deininger, P.L., Satchwell, S.C., Baer, R., Farrell, P.J.
             and Barrell, B.G.
   TITLE
             DNA sequence analysis of the EcoRI Dhet fragment of B95-8
             Epstein-Barr virus containing the terminal repeat sequences
   JOURNAL
             Mol. Biol. Med. 1 (4), 425-445 (1983)
   PUBMED
             6094955
REFERENCE
             10 (bases 45415 to 52824)
  AUTHORS
             Jones, M.D., Foster, L., Sheedy, T. and Griffin, B.E.
  TITLE
             The EB virus genome in Daudi Burkitt's lymphoma cells has a
             deletion similar to that observed in a non-transforming strain
             (P3HR-1) of the virus
  JOURNAL
             EMBO J. 3 (4), 813-821 (1984)
   PUBMED
             6327290
REFERENCE
             11 (bases 87650 to 92703)
  AUTHORS
             Biggin, M., Farrell, P.J. and Barrell, B.G.
  TITLE
             Transcription and DNA sequence of the BamHI L fragment of B95-8
             Epstein-Barr virus
  JOURNAL
             EMBO J. 3 (5), 1083-1090 (1984)
   PUBMED
             6203743
REFERENCE
             12 (bases 7315 to 9312)
             Yates, J., Warren, N., Reisman, D. and Sugden, B.
  AUTHORS
  TITLE
             A cis-acting element from the Epstein-Barr viral genome that
             permits stable replication of recombinant plasmids in latently
             infected cells
  JOURNAL
             Proc. Natl. Acad. Sci. U.S.A. 81 (12), 3806-3810 (1984)
   PUBMED
             6328526
             13 (bases 76089 to 79808)
REFERENCE
  AUTHORS
             Gibson, T., Stockwell, P., Ginsburg, M. and Barrell, B.
  TITLE
            Homology between two EBV early genes and HSV ribonucleotide
            reductase and 38K genes
            Nucleic Acids Res. 12 (12), 5087-5099 (1984)
  JOURNAL
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PUBMED
            6330697
REFERENCE
            14 (bases 1 to 172281)
            Baer, R., Bankier, A.T., Biggin, M.D., Deininger, P.L., Fallell, P.J.,
  AUTHORS
            Gibson, T.J., Hatfull, G., Hudson, G.S., Satchwell, S.C., Seguin, C.,
            Tuffnell, P.S. and Barrell, B.G.
  TITLE
            DNA sequence and expression of the B95-8 Epstein-Barr virus genome
  JOURNAL
            Nature 310 (5974), 207-211 (1984)
   PUBMED
            6087149
REFERENCE
            15
  AUTHORS
            Bodescot, M. and Perricaudet, M.
  TITLE
            Clustered alternative splice sites in Epstein-Barr virus RNAs
  JOURNAL
            Nucleic Acids Res. 15 (14), 5887 (1987)
   PUBMED
            3039467
REFERENCE
            16
  AUTHORS
            Laux, G., Perricaudet, M. and Farrell, P.J.
            A spliced Epstein-Barr virus gene expressed in immortalized
  TITLE
            lymphocytes is created by circularization of the linear viral
            genome
  JOURNAL
            EMBO J. 7 (3), 769-774 (1988)
   PUBMED
            2840285
REFERENCE
  AUTHORS
            Hatfull, G.F., Barrell, B.G., Quinn, J. and McGeoch, D.
  JOURNAL
            Unpublished
REFERENCE
            18 (bases 1 to 172281)
  AUTHORS
            Farrell, P.J. and Barrell, B.G.
  TITLE
            Direct Submission
  JOURNAL
            Submitted (05-JUN-1984)
REFERENCE
            19 (bases 1 to 172281)
  AUTHORS
            Farrell, P.J.
  TITLE
            Direct Submission
            Submitted (18-MAR-1988) Farrell P., Ludwig Institute for Cancer
  JOURNAL
            Research, St. Mary's Hospital Medical School, Norfolk Place London
COMMENT
            On or before Apr 23, 2004 this sequence version replaced gi:330432,
            gi:330357, gi:330413.
            CDS
            Listed under this feature are all known protein coding regions as
            well as all the major open reading frames in the sequence. In
            general the term major is taken as the longest frame in a
            particular region taking into account the adjacent longest frames
            and likely transcription signals. Note that on this basis some long
            overlapping frames have been excluded and on the other hand some
            small frames have been included which might represent exons or
            genes because they occur in a logical combination with other
            features or because of some other experimental data. The reading
            frames are named according to the Bam H1 fragment in which they
            start. eg BALF3 is the third leftward frame starting in Bam H1
            fragment A. BORF1 is the first rightward frame in Bam H1 fragment
            O. If there is an obvious TATA sequence followed by an in frame Met
            codon that satisfies the rules of Kozak [12] in that there is a
            purine at -3 and/or a G at +4 then the reading frame is numbered
            from the A of the ATG to the base preceding the termination codon.
            If there is no obvious initiation codon or there is a substantial
            reading frame in phase before the ATG then the reading frame is
            numbered from the first base of the first codon.
            SITEs of POLYA signals
            This feature lists all occurences of the sequence AATAAA which is
            found normally approximately 20 bases upstream of the mRNA
            processing/polyA addition site. The rarely used homolog ATTAAA is
```

major reading frame.

only listed when it is found in a position close to the end of a

SITEs of DONOR and ACCEPT sequences

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This is not a comprehensive listing of all such sequences and only
            the positions of a few have been noted because they occur in
            potentially interesting positions. The number quoted in the table
            is the position of the terminal base in the intron in each case.
            Restriction enzyme SITEs.
            Only the positions of the sites Bam HI (BAM) are listed. RPT
            This feature is used to define repetitive sequences. SITE DEL
            This feature defines deletions in B95-8 with respect to other
            strains such as RAJI and also to deletions in other strains such as
            P3HR1 and DAUDI with respect to B95-8.
           Denotes sequences with twofold symmetry ie could form hairpin
           loops. This is not a comprehensive list - only a few occurences
           noted.
           ORGRPL
           Denotes the region that encompasses an origin of replication (ori
           P).[13].
           NUMBERING
           The DNA sequence of B95-8 EBV has been revised [19]. The original
            (Baer et al, 1984) base 359 has been deleted so the new sequence
           around that position reads TCAGTCTTT. To avoid renumbering the
           entire sequence, position 1 has benn moved 1 base to the left of
           the EcoRI site separating EcoRI Dhet from EcoRI I
            (ie the first A of AGAATTC).
FEATURES
                    Location/Qualifiers
     source
                    1. .172281
                    /organism="Human herpesvirus 4"
                    /mol type="genomic DNA"
                    /strain="B95-8"
                    /db xref="taxon:10376"
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                    58. .272
                    /product="exon 2 terminal protein RNA"
    mRNA
                    360. .458
                    /product="exon 3 terminal protein RNA"
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                    complement (535)
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    mRNA
                    540. .788
                    /product="exon 4 terminal protein RNA"
    mRNA
                    871. .951
                    /product="exon 5 terminal protein RNA"
    mRNA
                    1026. .1196
                    /product="exon 6 terminal protein RNA"
    promoter
                    complement (1192)
                    /note="TATA: TATAAAT"
    mRNA
                    1280. .1495
                    /product="exon 7 terminal protein RNA"
    promoter
                    complement (1383)
 Query Match
                         100.0%;
                                 Score 1038;
                                              DB 13;
                                                     Length 172281;
 Best Local Similarity 100.0%; Pred. No. 0;
 Matches 1038; Conservative
                               0; Mismatches
                                                 0;
                                                     Indels
Qу
           1 ATGCTATCAGGTAACGCAGGAGAAGGAGCAACAGCCTGCGGAGGTTCGGCCGCCGCGGGC 60
             148707 ATGCTATCAGGTAACGCAGGAGAAGGAGCAACAGCCTGCGGAGGTTCGGCCGCGGGGC 148766
Db
          61 CAGGACCTCATCAGCGTCCCCCGCAACACCTTTATGACACTGCTTCAGACCAACCTGGAC 120
Qу
             148767 CAGGACCTCATCAGCGTCCCCCGCAACACCTTTATGACACTGCTTCAGACCAACCTGGAC 148826
Db
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Qу		AACAAACCGCCGAGGCAGACCCCGCTACCCTACGCGGCCCCGCTGCCCCCTTTTCCCAC	
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            Gibson, T.J., Hatfull, G.F., Hudson, G.S., Satchwell, S.C., Seguin, C.,
            Tuffnell, P.S. and Barrell, B.G.
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            DNA sequence and expression of the B95-8 Epstein-Barr virus genome
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            Nature 310 (5974), 207-211 (1984)
   PUBMED
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            Parker, B.D., Bankier, A., Satchwell, S., Barrell, B. and Farrell, P.J.
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            Sequence and transcription of Raji Epstein-Barr virus DNA spanning
            the B95-8 deletion region
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  JOURNAL
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  AUTHORS
            Sample, J., Brooks, L., Sample, C., Young, L., Rowe, M., Gregory, C.,
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  TITLE
            Restricted Epstein-Barr virus protein expression in Burkitt
            lymphoma is due to a different Epstein-Barr nuclear antigen 1
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            Proc. Natl. Acad. Sci. U.S.A. 88 (14), 6343-6347 (1991)
  JOURNAL
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  JOURNAL
            Unpublished (1992)
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     "The BamHI F region of the B95-8 Epstein-Barr virus genome.";
RL
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     Copyrighted by the UniProt Consortium, see http://www.uniprot.org/terms
     Distributed under the Creative Commons Attribution-NoDerivs License
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of the P3HR-1 deletion junction and characterization of the NotI
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            Transcription and DNA sequence of the BamHI L fragment of B95-8
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            Clustered alternative splice sites in Epstein-Barr virus RNAs
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            A spliced Epstein-Barr virus gene expressed in immortalized
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JOURNAL
            Virology 179 (1), 339-346 (1990)
   PUBMED
            2171209
REFERENCE
            18 (bases 1 to 171823)
            Hatfull, G.F., Barrell, B.G., Quinn, J. and McGeoch, D.
  AUTHORS
  JOURNAL
            Unpublished
REFERENCE
  AUTHORS
            Binne, U.K., Amon, W. and Farrell, P.J.
  TITLE
            Induction of Epstein-Barr virus late promoters on small plasmids in
            the EBV late lytic cycle requires ori lyt
  JOURNAL
            Unpublished
REFERENCE
            20 (bases 1 to 171823)
 AUTHORS
            Farrell, P.J.
  TITLE
            Direct Submission
  JOURNAL
            Submitted (01-AUG-2002) Farrell P., Ludwig Institute for Cancer
            Research, Imperial College School of Medicine, St. Mary's Campus,
            Norfolk Place London W2 1PG
COMMENT
            Construction:
            This sequence was assembled from B95-8 EBV [14] and Raji EBV [18]
            with sequence corrections [16, 19]. The number of major internal
            repeat units has been reduced from 11.6 [14] to a more typical 7.6
            and the B95-8 deletion sequences have been restored to give a
            sequence more representative of wild type EBV.
            Like the modified B95-8 sequence[14, 16] accession number V01555,
            this sequence starts 1 base to the left of the EcoRI site
            separating EcoRI Dhet from EcoRI I (ie the first A of AGAATTC.).
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RESULT 8
EBV
LOCUS
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                                               DNA
                                                       circular VRL 18-APR-2005
DEFINITION
           Epstein-Barr virus (EBV) genome, strain B95-8.
ACCESSION
            V01555 J02070 K01729 K01730 V01554 X00498 X00499 X00784
VERSION
            V01555.1 GI:59074
            DNA polymerase; EBNA; genome; ribonucleotide reductase; tandem
KEYWORDS
            repeat; terminal repeat.
SOURCE
            Human herpesvirus 4 (Epstein-Barr virus)
  ORGANISM
            Human herpesvirus 4
            Viruses; dsDNA viruses, no RNA stage; Herpesviridae;
            Gammaherpesvirinae; Lymphocryptovirus.
REFERENCE
  AUTHORS
            Arrand, J.R., Rymo, L., Walsh, J.E., Bjorck, E., Lindahl, T. and
            Griffin, B.E.
  TITLE
            Molecular cloning of the complete Epstein-Barr virus genome as a
            set of overlapping restriction endonuclease fragments
  JOURNAL
            Nucleic Acids Res. 9 (13), 2999-3014 (1981)
   PUBMED:
            6269068
REFERENCE
            2
  AUTHORS
            Kozak, M.
  TITLE
            Possible role of flanking nucleotides in recognition of the AUG
            initiator codon by eukaryotic ribosomes
  JOURNAL
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REFERENCE
  AUTHORS
          Deininger, P.L., Bankier, A., Farrell, P., Baer, R. and Barrell, B.
  TITLE
            Sequence analysis and in vitro transcription of portions of the
            Epstein-Barr virus genome
  JOURNAL
            J. Cell. Biochem. 19 (3), 267-274 (1982)
            6296170
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  AUTHORS
            Farrell, P.J., Bankier, A., Seguin, C., Deininger, P. and Barrell, B.G.
  TITLE
            Latent and lytic cycle promoters of Epstein-Barr virus
  JOURNAL
            EMBO J. 2 (8), 1331-1338 (1983)
            10872327
  PUBMED
REFERENCE
  AUTHORS
            Farrell, P.J., Deininger, P.L., Bankier, A. and Barrell, B.
            Homologous upstream sequences near Epstein-Barr virus promoters
  TITLE
  JOURNAL
            Proc. Natl. Acad. Sci. U.S.A. 80 (6), 1565-1569 (1983)
   PUBMED
            6300857
REFERENCE
               (bases 142687 to 159853)
  AUTHORS
            Bankier, A.T., Deininger, P.L., Farrell, P.J. and Barrell, B.G.
  TITLE
            Sequence analysis of the 17,166 base-pair EcoRI fragment C of B95-8
            Epstein-Barr virus
  JOURNAL
           Mol. Biol. Med. 1 (1), 21-45 (1983)
   PUBMED
            6092825
REFERENCE
            7
               (bases 112620 to 125316)
 AUTHORS
            Seguin, C., Farrell, P.J. and Barrell, B.G.
  TITLE
            DNA sequence and transcription of the BamHI fragment B region of
            B95-8 Epstein-Barr virus
  JOURNAL
           Mol. Biol. Med. 1 (3), 369-392 (1983)
  PUBMED
            6094953
REFERENCE
               (bases 45644 to 52450)
 AUTHORS
            Jeang, K.T. and Hayward, S.D.
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